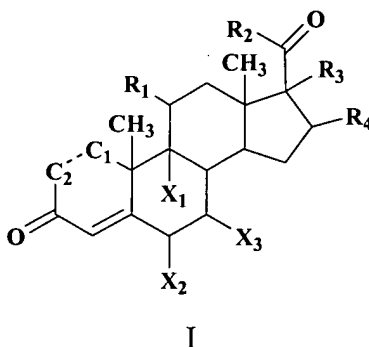<u>AMENDMENTS TO THE CLAIMS</u>

Please amend the claims as provided in the following claims listing:

<u>Claims Listing:</u>

1. (withdrawn) A corticosteroid conjugate comprising a corticosteroid attached to a group that is either a bulky group of greater than 400 daltons or a charged group of less than 400 daltons, wherein said corticosteroid conjugate has anti-inflammatory activity *in vivo* and reduced activity in the central nervous system in comparison to said corticosteroid without said group.

2. (withdrawn) The corticosteroid conjugate of claim 1, wherein said corticosteroid is covalently attached via a linker to said group.

3. (withdrawn) The corticosteroid conjugate of claim 2 having formula I:

I

wherein

the bond between C_1 and C_2 is a double or a single bond;
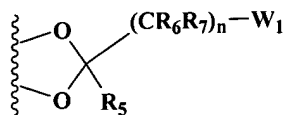
X_1 represents -H or a halogen atom;

X_2 represents -H, -CH$_3$, or a halogen atom;

X_3 represents -H or a halogen atom;

R_1 represents =O or –OH;

R_2 represents -CH$_3$, -SCH$_2$F, -CH$_2$Cl, -CH$_2$-G, -CH$_2$OH, -CH$_2$O-P(O)(O$^-$)$_2$, CH$_2$O-acyl, -CH$_2$NH-G^1, -CH$_2$S-G^1, or -CH$_2$O-G^1;

R_3 and R_4 each, independently, represents -H, C_{1-10} alkyl, -OH, -O-acyl, -O-G^1, or R_3 and R_4 combine to form a cyclic acetal of formula II wherein:

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$$\text{(structure II: a cyclic diether with a quaternary carbon bearing } R_5 \text{ and } (CR_6R_7)_n{-}W_1)$$

II

n is an integer from 0 to 6;

R_5, R_6, and R_7 each, independently, represents -H or C_{1-10} alkyl;

W_1 represents -H, -CH$_3$, -G^1, -NR$_8$-G^1, –NH-NH-G^1, -O-G^1, -S-G^1, -C(O)-G^1, or -C(S)-G^1;

R_8 represents -H, C_{1-10} alkyl or C_{5-10} aryl; and

G^1 is a bond between said corticosteroid and said linker.

4. (withdrawn) The corticosteroid conjugate of claim 3, wherein said linker is described by formula III:

$$G^1\text{-}(Z^1)_o\text{-}(Y^1)_u\text{-}(Z^2)_s\text{-}(R_{10})\text{-}(Z^3)_t\text{-}(Y^2)_v\text{-}(Z^4)_p\text{–}G^2$$

III

wherein

G^1 is a bond between said corticosteroid and said linker;

G^2 is a bond between said linker and said bulky group or between said linker and said charged group;

Z^1, Z^2, Z^3, and Z^4 each, independently, is selected from O, S, and NR_{11};

R_{11} is hydrogen or a C_{1-10} alkyl group;

Y^1 and Y^2 are each, independently, selected from carbonyl, thiocarbonyl, sulphonyl, or phosphoryl;

o, p, s, t, u, and v are each, independently, 0 or 1; and

R_{10} is a C_{1-10} alkyl, a linear or branched heteroalkyl of 1 to 10 atoms, a linear or branched C_{2-10} alkene, a linear or branched C_{2-10} alkyne, a C_{5-10} aryl, a cyclic system of 3 to 10 atoms, -(CH$_2$CH$_2$O)$_q$CH$_2$CH$_2$- in which q is an integer of 1 to 4, or a chemical bond linking G^1-$(Z^1)_o$-$(Y^1)_u$-$(Z^2)_s$- to -$(Z^3)_t$-$(Y^2)_v$-$(Z^4)_p$–G^2.

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5. (withdrawn) The corticosteroid conjugate of claim 1, wherein said bulky group comprises a naturally occurring polymer or a synthetic polymer.

6. (withdrawn) The corticosteroid conjugate of claim 5, wherein said naturally occurring polymer is a glycoprotein, a polypeptide, or a polysaccharide.

7. (withdrawn) The corticosteroid conjugate of claim 5, wherein said bulky group comprises hyaluronic acid or alpha-1-acid glycoprotein.

8. (withdrawn) The corticosteroid conjugate of claim 5, wherein said synthetic polymer is a polyethylene glycol or N-hxg.

9. (withdrawn) The corticosteroid conjugate of claim 1, wherein said charged group is a polyanion comprising at least three negatively charged moieties.

10. (withdrawn) The corticosteroid conjugate of claim 1, wherein said charged group is a cation.

11. (withdrawn) The corticosteroid conjugate of claim 1, wherein said bulky group comprises a corticosteroid.

12. (amended) A method of treating an autoimmune or inflammatory condition in a mammal, said method comprising administering to said mammal a corticosteroid conjugate ~~of claim 1~~ comprising a corticosteroid attached to a group that is either a bulky group of greater than 400 daltons or a charged group of less than 400 daltons in an amount effective to treat said condition, wherein said corticosteroid conjugate has anti-inflammatory activity *in vivo* and reduced activity in the central nervous system in comparison to said corticosteroid without said group.

13. (original) The method of claim 12, wherein said condition is selected from the group consisting of asthma, psoriasis, eczema, organ/tissue transplant rejection, graft vs. host reactions, Raynaud's syndrome, autoimmune thyroiditis, Grave's disease, autoimmune hemolytic anemia, autoimmune thromboeytopenia purpura, mixed connective tissue disease, idiopathic Addison's disease, Sjogren's syndrome, urticaria, dermatitis, multiple sclerosis, rheumatoid arthritis, insulin-dependent diabetes mellitus, uveitis, Crohn's disease, ulcerative colitis, lupus, tendonitis, bursitis, adult respiratory distress syndrome, shock, oxygen toxicity, glomerulonephritis, vasculitis, reactive arthritis, necrotizing enterocolitis, Goodpasture's syndrome, hypersensitivity pneumonitis, glomerulonephritis; encephalomyelitis, and meningitis.

14. (original) The method of claim 12, wherein said condition is rheumatoid arthritis or colitis.

15. (original) The method of claim 12, wherein said corticosteroid conjugate is administered by intravenous, intraperitoneal, subcutaneous, ocular, topical, nasal, or intramuscular administration.
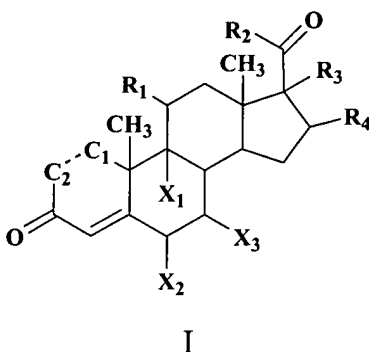
16. (withdrawn) A method for inhibiting passage across the blood-brain barrier of a corticosteroid, said method comprising covalently attaching a group that is a bulky group of greater than 400 daltons or a charged group of less than 400 daltons, wherein said group increases the size, or alters the charge, of the corticosteroid sufficiently to inhibit passage across the blood-brain barrier without destroying the anti-inflammatory activity of said corticosteroid.

17. (withdrawn) The method of claim 16, wherein said group is covalently linked via one or more of positions C16, C17, and C21 of said corticosteroid.

18. (withdrawn) A pharmaceutical composition comprising an effective amount of a corticosteroid conjugate of claim 1, together with a pharmaceutically acceptable carrier or diluent.

19. (new) The method of claim 12, wherein said corticosteroid is covalently attached via a linker to said group.

20. (new) The method of claim 19, having formula I:

I

wherein

the bond between C_1 and C_2 is a double or a single bond;

X_1 represents -H or a halogen atom;

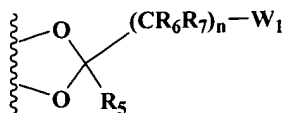X_2 represents -H, $-CH_3$, or a halogen atom;

X_3 represents -H or a halogen atom;

R_1 represents =O or –OH;

R_2 represents $-CH_3$, $-SCH_2F$, $-CH_2Cl$, $-CH_2$-G, $-CH_2OH$, $-CH_2O-P(O)(O^-)_2$, CH_2O-acyl, $-CH_2NH-G^1$, $-CH_2S-G^1$, or $-CH_2O-G^1$;

R_3 and R_4 each, independently, represents -H, C_{1-10} alkyl, -OH, -O-acyl, $-O-G^1$, or R_3 and R_4 combine to form a cyclic acetal of formula II wherein:

$$\text{(CR}_6\text{R}_7)_n\text{—W}_1$$

II

n is an integer from 0 to 6;

R_5, R_6, and R_7 each, independently, represents -H or C_{1-10} alkyl;

W_1 represents -H, -CH$_3$, -G^1, -NR$_8$-G^1, –NH-NH-G^1, -O-G^1, -S-G^1, -C(O)-G^1, or -C(S)-G^1;

R_8 represents -H, C_{1-10} alkyl or C_{5-10} aryl; and

G^1 is a bond between said corticosteroid and said linker.

21. (new) The method of claim 20, wherein said linker is described by formula III:

$$G^1\text{-}(Z^1)_o\text{-}(Y^1)_u\text{-}(Z^2)_s\text{-}(R_{10})\text{-}(Z^3)_t\text{-}(Y^2)_v\text{-}(Z^4)_p\text{–}G^2$$

III

wherein

G^1 is a bond between said corticosteroid and said linker;

G^2 is a bond between said linker and said bulky group or between said linker and said charged group;

Z^1, Z^2, Z^3, and Z^4 each, independently, is selected from O, S, and NR$_{11}$;

R_{11} is hydrogen or a C_{1-10} alkyl group;

Y^1 and Y^2 are each, independently, selected from carbonyl, thiocarbonyl, sulphonyl, or phosphoryl;

o, p, s, t, u, and v are each, independently, 0 or 1; and

R_{10} is a C_{1-10} alkyl, a linear or branched heteroalkyl of 1 to 10 atoms, a linear or branched C_{2-10} alkene, a linear or branched C_{2-10} alkyne, a C_{5-10} aryl, a cyclic system of 3 to 10 atoms, -(CH$_2$CH$_2$O)$_q$CH$_2$CH$_2$- in which q is an integer of 1 to 4, or a chemical bond linking G^1-(Z^1)$_o$-(Y^1)$_u$-(Z^2)$_s$- to -(Z^3)$_t$-(Y^2)$_v$-(Z^4)$_p$–G^2.

22. (new) The method of claim 12, wherein said bulky group comprises a naturally occurring polymer or a synthetic polymer.

23. (new) The method of claim 22, wherein said naturally occurring polymer is a glycoprotein, a polypeptide, or a polysaccharide.

24. (new) The method of claim 22, wherein said bulky group comprises hyaluronic acid or alpha-1-acid glycoprotein.

25. (new) The method of claim 22, wherein said synthetic polymer is a polyethylene glycol or N-hxg.

26. (new) The method of claim 12, wherein said charged group is a polyanion comprising at least three negatively charged moieties.

27. (new) The method of claim 12, wherein said charged group is a cation.

28. (new) The method of claim 12, wherein said bulky group comprises a corticosteroid.